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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/996,620	11/27/2001	Amechand Boodhoo	8702.0001.03	5369

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EXAMINER
PROUTY, REBECCA E

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/996,620	Boodhoo et al.
Examiner	**Art Unit**
Rebecca Prouty	1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 30, 2003*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-21, 27-31, 37-41, 47-51, 57-61, 67-71, 77-81, 87-89, and 96-9* is/are pending in the application.

4a) Of the above, claim(s) *8-10, 13-15, and 96-99* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-7, 11, 12, 16-21, 27-31, 37-41, 47-51, 57-61, 67-71, 77-81, and 87* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Claims 22-26, 32-36, 42-46, 52-56, 62-66, 72-76, 82-86 and 90-95 have been canceled. Claims 1-21, 27-31, 37-41, 47-51, 57-61, 67-71, 77-81, 87-89 and 96-99 are at issue and are present for examination.

Applicant's election with traverse of Group I, Claims 1-7, 11, 12, 16-21, 27-31, 37-41, 47-51, 57-61, 67-71, 77-81, and 87-89 in Paper No. 10 is acknowledged. The traversal is on the ground(s) that there would be no additional burden of search for the coexamination of all groups as any reference describing treatments with mocarhagin, methods of isolating mocarhagin or antibodies thereto would also describe the protein itself. This is not found persuasive because each of the restricted groups would require search for subject matter unnecessary for the search of the elected group. Even if applicants statement that any reference describing treatments with mocarhagin, methods of isolating mocarhagin or antibodies thereto would also describe the protein itself were true, not all references describing the protein will describe nor make obvious treatments with mocarhagin, methods of isolating mocarhagin or antibodies thereto. The additional search required to address the additional groups would be substantial and constitute an undue burden on the Office.

The requirement is still deemed proper and is therefore made FINAL.

Claims 8-10, 13-15, and 96-99 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10.

Claims 11 and 12 are objected to because of the following informalities: these claims depend from non-elected claims. Appropriate correction is required.

Claims 27, 37, 47, 57, 67, 77, and 87 are objected to because of the following informalities: the word "of should be inserted between "a culture" and "a host cell" in line 1 of step (a) of each of these claims. Appropriate correction is required.

Claims 31, 41, 51, 61, 71, and 81 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 31, 41, 51, 61, 71, and 81 depend from Claims 30, 40, 50, 60, 70, and 80 respectively but in each case recite a composition comprising the protein of SEQ ID NO:6 which is outside the scope of Claims 30, 40, 50, 60, 70, and 80. Claims 30, 40, 50, 60, 70, and 80 recite compositions comprising the

proteins of SEQ ID NOS: 8, 10, 12, 14, 16, and 18 or specific fragments thereof respectively. As SEQ ID NO:6 is different from each of SEQ ID NOS: 8, 10, 12, 14, 16, and 18, these claims are confusing and improperly dependent and/or duplicative of Claim 21.

Claims 1-7, 11-12 and 16-18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a genus of mocarhagin proteins. The term "mocarhagin protein" when read in light of applicants specification encompasses any cobra venom polypeptide which exhibits one of the functional activities recited on page 18, lines 1-12 or fragments thereof which retain the functional activity. It should be noted that the specification provides evidence that a single cobra species produces at least five distinct polypeptide sequences within the scope of this definition, and that a substantial number of distinct cobra species are well known. As such one of ordinary skill in the art would reasonably expect that the genus of full length "mocarhagin proteins" contains a large number of structurally distinct

proteins (as each cobra species would be reasonably expected to encode several such proteins) and the genus of "mocarhagin proteins" would be even larger when one considers the inclusion of functionally active fragments of all such full length proteins and that other cobra venom polypeptides which are structurally unrelated to the disclosed polypeptides may exhibit one or more of the recited activities. The specification teaches the structure of several mocarhagin proteins from only a single representative species of cobra. The specification fails to describe mocarhagin proteins from any other cobra species by any identifying characteristics or properties other than the functionality of being a mocarhagin protein. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Applicants are further advised that Claim 18 recites compositions of mocarhagin proteins having a particular amino terminal amino acid sequence (i.e., SEQ ID NO:2), however, none of the disclosed amino acid structures of mocarhagin proteins in fact encompass this amino-terminal sequence exactly. Applicants

are requested to verify that the amino acid sequence disclosed in the specification and sequence listing is in fact correct.

Claims 20, 21, 30, 31, 40, 41, 50, 51, 60, 61, 70, 71, 80 and 81 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention appears to employ novel clones. Since the clones are essential to the claimed invention, they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The claimed clones' sequences are not fully disclosed, nor have all the sequences required for their construction been shown to be publicly known and freely available. The enablement requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the clones. The specification does not disclose a repeatable process to obtain the clones and it is not apparent if the DNA sequences are readily available to the public. Accordingly, it is deemed that a deposit of these clones should have been made in accordance with 37 CFR 1.801-1.809.

It is noted that applicants have deposited the organisms but there is no indication in the specification as to public availability. If the deposit was made under the terms of the

Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, applicants may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

1. during the pendency of this application , access to the invention will be afforded to the Commissioner upon request;
2. all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
3. the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and
4. the deposit will be replaced if it should ever become inviable.

Claims 1-7, 11-12, 16-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for mocarhagin proteins comprising residues 192-621 of SEQ ID NO:8, 192-439 of SEQ ID NO:8, 192-613 of SEQ ID NO:10, 192-521 of SEQ ID NO:12, 192-592 of SEQ ID NO:14, 62-462 of SEQ ID NO:16, or 197-621 of SEQ ID NO:18, fragments thereof having mocarhagin activity or mocarhagin isolated by the process of Example 1 of the specification, does not reasonably provide enablement for any mocarhagin polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it

is most nearly connected, to make the invention commensurate in scope with these claims.

These claims are directed to a genus of mocarhagin proteins. The term "mocarhagin protein" when read in light of applicants specification encompasses any polypeptide isolated from cobra venom which exhibits one of the functional activities recited on page 18, lines 1-12 or fragments thereof which retain the functional activity. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of enzymes broadly encompassed by the claims. Neither the specification nor the prior art provide any expectation that any cobra venom protein having one of the activities recited on page 18, lines 1-12 could be isolated by using the methods taught in the specification. One of ordinary skill in the art would clearly be aware that proteins with similar activities can be highly diverse and often bear little or no homology to one another and thus would not be expected to be isolated by similar methods. Furthermore, while many different techniques for protein purification are known in the art, which techniques will be useful for purification of any individual protein is highly unpredictable absent any knowledge regarding the structural characteristics of the desired protein. As such one of ordinary skill in the art would be unable to isolate such

mocarhagin proteins without undue experimentation to find a suitable method of isolation. It should be noted that Claim 18 is included within this rejection as it recites an N-terminal sequence not present within any of the disclosed mocarhagin polypeptides and it is unclear if any mocarhagin polypeptide (i.e, naturally occurring cobra venom polypeptide) having this N-terminal sequence even exists. Furthermore, Claims 11-12 are included in the rejection as the methods recited in Claim 10 fail to recite specific details of the purification of example 1 including with what the affinity and Mono S columns are eluted, a recitation of whether "the eluate" in step (b) is the eluate that bound to the heparin affinity column or the unbound eluate, a recitation of what type of size exclusion column was used and a recitation of what fraction from the size exclusion column are "the eluate" added to the Mono S column in step (c). Without a recitation of these specifics of the purification procedure, the many methods recited in Claim 10 may result in many unrelated proteins. As the number of possible compounds which could be used to elute the affinity and Mono S columns is enormous, the number of possible size exclusion matrices is also large, and the only guidance in the specification as to which of these variables is likely to be successful in obtaining a mocarhagin protein is the method as taught in Example 1, it would require undue

experimentation to isolate any mocarhagin polypeptide encompassed by the broadly recited methods of Claim 10.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2, 4-7, 11, 12, 16-21, 27-31, 37-41, 47-51, 57-61, 67-71, 77-81, and 87-89 are rejected under 35 U.S.C. 102(b or e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Berndt et al. (US Patent 5,659,018) or De Luca et al.

Berndt et al. and De Luca et al. each teach the purification of mocarhagin from the venom of the Mozambiquan spitting cobra (*Naja mocambique mocambique*). The mocarhagin compositions obtained by Berndt et al. and De Luca et al. were isolated by a procedure identical to that of Claim 10 on the instant application except for the final Mono S column step, has an IC_{50}

of 0.1 μg/ml in a neutrophil/HL60 binding inhibition assay, a MW of 55 kDa, inhibits platelet binding to vWF, cleaves PGSL-1 and GPIBα. It is impossible for the examiner to determine if the disclosed compositions of Berndt et al. and De Luca et al. meet the claim limitation of "at least 95% free of other cobra proteins". Therefore, this rejection is made in the alternative under either 35 U.S.C. 102(b or e) or under 35 U.S.C. 103(a). In the event that the compositions of Berndt et al. and De Luca et al. do not meet the claim limitation of "at least 95% free of other cobra proteins", it would have been obvious to one of ordinary skill in the art to further purify the protein using standard protein purification techniques well known in the art as the need for high purity in proteins with pharmaceutical use is well known. Although the amino acid sequence of the mocarhagin preparation was not disclosed in the cited references in each case the composition was prepared using the same methods as those in the instant application from a crude venom mixture and thus inherently contains the mature forms of all of SEQ ID NOS:6, 8, 10, 12, 14, 16, and 18. Since the Office does not have the facilities for examining and comparing applicants' protein with the protein of the prior art compositions, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the

protein of the prior art compositions does not possess the same material structural and functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (703) 308-4000. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Rebecca Prouty
Primary Examiner
Art Unit 1652